

Applicants: Nancy Carrasco et al.
Serial No.: 09/519,959
Filed: March 7, 2000
page 2

REMARKS

Claims 1, 2, 6, 8, 9, 29, and 30 are pending and under consideration in the subject application.

Statement of Substance of July 8, 2003 Telephonic Interview with Examiner Rawlings

This Statement is submitted in fulfillment of the requirements of the Interview Summary attached to the July 11, 2003 Advisory Action.

On July 8, 2003, Examiner Rawlings telephoned the undersigned attorney to inform him that applicants' May 6, 2003 response to the April 8, 2003 Final Office Action had been entered and carefully considered but was not found persuasive. The references Spitzweg et al. and Cancroft et al. were briefly discussed by the Examiner. The Examiner stated that an Advisory Action would be prepared and mailed as soon as possible explaining more thoroughly the reasons that the arguments set forth in applicants' response were not favorably considered by the Examiner.

Applicants thank the Examiner for his July 8, 2003 telephone call.

Rejections under 35 U.S.C. §103(a)

In the Advisory Action issued July 11, 2003, the Examiner maintained the rejection first set forth in the April 8, 2003 Final Office Action of claims 1, 2, 6, 8, 9, 29, and 30 as obvious under 35 U.S.C. §103(a). The Examiner indicated that applicants' response filed on May 6, 2003 was not persuasive for the reasons discussed below. Applicants respectfully traverse this rejection.

First, the Examiner indicated that Spitzweg et al. teach that NIS is commonly expressed in the thyroid and other tissues, including the breast. Applicants agree that Spitzweg et al. teach the expression of NIS in normal, nonlactating breast tissue, as well as in the following normal tissues: thyroid gland, salivary gland, parotid gland,

Applicants: Nancy Carrasco et al.
Serial No.: 09/519,959
Filed: March 7, 2000
page 3

submandibular gland, pituitary gland, pancreas, testis, gastric mucosa, prostate, ovary, adrenal gland, heart, thymus, and lung (see page 1748, first paragraph, right column). In addition, Spitzweg et al. also cite Smanik et al. (1997) for reporting the detection of NIS expression in normal breast tissue, as well as in colon, ovary, and thyroid (see page 1750, first full paragraph, left column). A copy of Smanik et al. (Endocrinology 138: 3555-8, 1997) is attached hereto as **Exhibit 1**. Smanik et al. (1997) also teach that NIS expression is greatly reduced in thyroid tumors compared to normal thyroid tissue (see Abstract of Smanik et al., 1997). Applicants maintain that the observations noted above in the present paragraph teach away from the subject invention. That is, reports of NIS expression in normal tissue, including normal breast tissue (Spitzweg et al., Smanik et al. 1997), and of a large reduction in NIS expression in tumors of the thyroid compared to normal thyroid tissue (Smanik et al., 1997), teach away from the present invention that expression of mgNIS in nonlactating breast tissue is indicative of the presence of breast cancer in the subject.

Next, the Examiner stated that Spitzweg et al. teach that many tissues, including breast tissue, share the capacity of the thyroid gland to actively accumulate pertechnetate and radioiodide by the activity of NIS. Applicants respectfully submit that this statement is a mischaracterization of the teachings of Spitzweg et al. First, applicants cannot find where Spitzweg et al. even mention the word "pertechnetate." Next, in regard to radioiodide, applicants maintain that Spitzweg et al. leave open the possibilities that radioiodide is taken up by the breast by (1) "nonspecific" mechanisms, (2) NIS, or (3) a combination of "nonspecific" mechanisms and NIS. Applicants direct the Examiner's attention to the discussion on page 1750, left column, where Spitzweg et al. first make the point that (emphasis added):

Applicants: Nancy Carrasco et al.
Serial No.: 09/519,959
Filed: March 7, 2000
page 4

Whole-body scintigraphy with radioiodine-131, an important diagnostic test in the management of patients with differentiated thyroid cancer, has revealed false-positive uptake in a significant number of cases.

Then, after pointing out that radioiodine uptake has been noted in a variety of normal and abnormal thyroid tissues, including the nonlactating mammary gland, Spitzweg et al. state (emphasis added):

Although iodide uptake by these extrathyroid tissues may result from nonspecific iodide accumulation, our detection of significant quantities of hNIS gene expression in thyroid gland, salivary glands, thymus, pituitary gland, pancreas, testis, mammary gland, and gastric mucosa, and of lower degrees of NIS gene expression in prostate, ovary, adrenal gland, lung, heart, and nasopharyngeal mucosa suggests that iodide transport in some of these tissues may be a specific property conferred by the expression of NIS.

Thus, although Spitzweg et al. suggest the possibility that radioiodide uptake in some extrathyroid tissues may involve NIS, Spitzweg et al. at best represent an invitation to experiment to determine the extent to which different mechanisms are involved in radioiodide uptake in different extrathyroid tissues.

The Examiner then goes on to conclude that Spitzweg et al. thus teach the nexus between NIS expression in the breast and the NIS-mediated accumulation of pertechnetate and radioiodide by the breast, which leads one to the conclusion that in the method of Cancroft et al., one is determining in effect, whether or not NIS is more or less abundantly expressed in the subject's breast tissue. Applicants maintain that this conclusion is based on a mischaracterization of the teachings of Spitzweg et al. and that, as discussed above, Spitzweg et al. both teach away from the subject invention and at best, present an invitation to further experimentation. In addition, applicants also note that Cancroft et al. observed pertechnetate uptake and not radioiodide uptake, that

Applicants: Nancy Carrasco et al.
Serial No.: 09/519,959
Filed: March 7, 2000
page 5

applicants cannot find a teaching concerning pertechnetate uptake in Spitzweg et al., and that Cancroft et al. state that "[t]he mechanism of ^{99m}Tc -pertechnetate concentration in malignant breast masses is not clear." (See Cancroft et al., p. 444, left column.)

Applicants maintain that the combination of Spitzweg et al. and Cancroft et al. do not teach that the expression of mgNIS in the breast tissue of a nonlactating subject is indicative of the presence of breast cancer in the subject and thus that the combination of Spitzweg et al. and Cancroft et al. does not render obvious applicants' invention.

In summary, the references cited by the Examiner neither teach nor suggest each and every element of the claimed invention and do not render obvious the subject matter as a whole for which patent protection is sought. Accordingly, reconsideration and withdrawal of the ground of rejection under 35 U.S.C. §103(a) is respectfully requested.

Conclusion

In light of the above discussion, applicants respectfully request reconsideration of the Examiner's remarks in the July 11, 2003 Advisory Action, withdrawal of the rejection set forth in the April 8, 2003 Final Office Action and passage of pending claims 1, 2, 6, 8, 9, 29, and 30 to allowance. If there are any minor matters that would prevent allowance of the claims, applicants request that the Examiner contact the undersigned attorney.

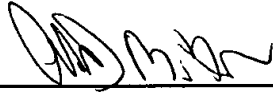
Applicants: Nancy Carrasco et al.
Serial No.: 09/519,959
Filed: March 7, 2000
page 6

A check in the amount of \$430.00 is enclosed to cover the fees for a small entity for filing a Request for Continued Examination under 37 C.F.R. §1.114 (\$375.00) and for a one month extension of time (\$55.00). It is believed that no additional fee is required to maintain the pendency of the subject application. However, if there are any unanticipated fees required to maintain the pendency of this application, the PTO is authorized to withdraw those fees from Deposit Account 01-1785.

Respectfully submitted,

AMSTER, ROTHSTEIN & EBENSTEIN
Attorneys for Applicants
90 Park Avenue
New York, New York 10016
(212) 697-5995

Dated: New York, New York
August 8, 2003

By: 
Craig J. Arnold, Registration No. 34,287
Alan D. Miller, Registration No. 42,889